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NEWS 14 Dec 10 WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
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NEWS 16 Dec 17 WELDASEARCH now available on STN
NEWS 17 Dec 17 STANDARDS now available on STN
NEWS 18 Dec 17 New fields for DPCI
NEWS 19 Dec 19 CAS Roles modified
NEWS 20 Dec 19 1907-1946 data and page images added to CA and Caplus
NEWS 21 Jan 25 BLAST(R) searching in REGISTRY available in STN on the Web
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NEWS 23 Jan 29 FSTA has been reloaded and moves to weekly updates
NEWS 24 Feb 01 DKILIT now produced by FIZ Karlsruhe and has a new update
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NEWS 25 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 26 Mar 08 Gene Names now available in BIOSIS

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CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
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L1 160 LONBERG N7/AU OR KAY/AU

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L2 16 L1 AND CD4

=> dup rem l2
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=> dis l3 1-11 ibib abs

L3 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:152726 CAPLUS
DOCUMENT NUMBER: 134:206569
TITLE: Human CTLA-4 antibodies and their uses
INVENTOR(S): Korman, Alan J.; Halk, Edward L.; Lonberg, Nils
PATENT ASSIGNEE(S): Medarex, Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014424	A2	20010301	WO 2000-US23356	20000824
WO 2001014424	A3	20010920		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-150452 P 19990824

AB The present invention provides novel human sequence antibodies against human CTLA-4 and methods of treating human diseases (e.g. cancer, allergy, inflammation, autoimmune disease, graft vs. host disease, Alzheimer's disease), infections and other conditions using these antibodies.

L3 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:741488 CAPLUS
DOCUMENT NUMBER: 135:302905
TITLE: Transgenic non-human animals for producing human antibodies specific for human antigens
INVENTOR(S): Lonberg, Nils; Kay, Robert M.
PATENT ASSIGNEE(S): Genpharm International, USA
SOURCE: U.S., 314 pp., Cont.-in-part of U.S. Ser. No. 728,463.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6300129	B1	20011009	US 1996-758417	19961202
EP 814159	A2	19971229	EP 1997-201755	19910828
EP 814159	A3	19990714		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
JP 11206387 A2 19990803 JP 1998-126859 19910828
US 5569825 A 19961029 US 1991-810279 19911217
US 5789650 A 19980804 US 1992-853408 19920318
US 5545806 A 19960813 US 1992-990860 19921216
US 5814318 A 19980929 US 1993-96762 19930722
JP 08140528 A2 19960604 JP 1994-289067 19941028
US 5625126 A 19970429 US 1994-352322 19941207
US 5770429 A 19980623 US 1995-544404 19951010
WO 9824884 A1 19980611 WO 1997-US21803 19971201
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9856881	A1	19980629	AU 1998-56881	19971201
EP 942959	A1	19990922	EP 1997-953058	19971201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LV, FI, RO				
JP 2001527386	T2	20011225	JP 1998-525687	19971201
US 6255458	B1	20010703	US 1998-42353	19980313

PRIORITY APPLN. INFO.: US 1990-574748 B2 19900829

US 1990-575962 B2 19900831
US 1991-810279 A2 19911217
US 1992-853408 A2 19920318
US 1992-904068 B2 19920623
US 1992-990860 A2 19921216
US 1993-53131 A2 19930426
US 1993-96762 A2 19930722
US 1993-155301 B2 19931118
US 1993-161739 B2 19931203
US 1993-165699 B2 19931210
US 1994-209741 B2 19940309
US 1994-352322 A2 19941207
US 1995-544404 A2 19951010
US 1996-728463 A2 19961010
EP 1991-916470 A3 19910828
JP 1991-515142 A3 19910828
WO 1991-US6185 A 19910828
US 1992-834539 A2 19920205
WO 1992-US10983 A 19921217
WO 1994-US4580 A 19940425
US 1996-758417 A 19961202
WO 1997-US21803 W 19971201

AB The invention relates to transgenic non-human animals capable of producing heterologous antibodies and methods for producing human sequence antibodies which bind to human antigens with substantial affinity. Transgenes contg. all or portions of the human Ig heavy and light chain loci, or transgenes contg. synthetic "miniloci" which comprise essential functional elements of the human heavy and light chain loci, are employed to produce a transgenic nonhuman animal. Such a transgenic nonhuman animal has the capacity to produce Ig chains that are encoded by human Ig genes, and addnl. are capable of making an immune response against human antigens. Such transgenic animals can serve as a source of immune sera reactive with specified human antigens, and B-cells from such transgenic animals can be fused with myeloma cells to produce hybridomas that secrete monoclonal antibodies that are encoded by human Ig genes and which are

specifically reactive with human antigens. Thus, functional human light chain V segments are successfully introduced into the mouse genome by co-injection of a human .kappa. light chain minilocus and a YAC clone comprise multiple human V78 segments. The V78 segment genes contained on the YAC contribute to the expressed repertoire of human .kappa. chains in the resultant mouse. This example demonstrates a method for the repertoire expansion of transgene-encoded human Ig proteins, and specifically shows how a human .kappa. chain variable region repertoire can be expanded by co-introduction of unlinked polynucleotides comprising human Ig variable region segments.

REFERENCE COUNT: 123 THERE ARE 123 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:594996 CAPLUS
DOCUMENT NUMBER: 131:227650
TITLE: Recombination and class switch for human immunoglobulin transgenes in mouse
INVENTOR(S): Lonberg, Nils; Fishwild, Dianne M.; Ball, William J., Jr.
PATENT ASSIGNEE(S): Genpharm International, Inc., USA
SOURCE: PCT Int. Appl., 484 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945962	A1	19990916	WO 1999-US5535	19990312
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 11206387	A2	19990803	JP 1998-126859	19910828
US 6255458	B1	20010703	US 1998-42353	19980313
AU 9930864	A1	19990927	AU 1999-30864	19990312

PRIORITY APPLN. INFO.:
US 1998-42353 A1 19980313
US 1990-574748 B2 19900829
US 1990-575962 B2 19900831
JP 1991-515142 A3 19910828
US 1991-810279 A2 19911217
US 1992-834539 A2 19920205
US 1992-853408 A2 19920318
US 1992-904068 B2 19920623
US 1992-990860 A2 19921216
US 1993-53131 A2 19930426
US 1993-96762 A2 19930722
US 1993-155301 B2 19931118
US 1993-161739 B2 19931203
US 1993-165699 B2 19931210
US 1994-209741 B2 19940309
US 1994-352322 A2 19941207
US 1995-544404 A2 19951010
US 1996-728463 A2 19961010
US 1996-758417 A2 19961202
WO 1999-US5535 W 19990312

AB The authors disclose the generation of transgenic non-human animals (i.e., mice) capable of producing heterologous human antibodies. The transgenic mice exhibit V(D)J recombination, class switching, and affinity maturation in response to immunization. Endogenous gene expression is prevented by homologous recombination or other ablative or suppressive methods. In one example, mice bearing human heavy chain transgenes and immunized with human carcinoembryonic antigen produced CEA-specific IgM. In a second example, mice bearing both heavy chain and light chain transgenes and immunized with human CD4 produced a primary anti-CD4 IgM response and, on subsequent reimmunization, a secondary anti-CD4 IgG response.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:398397 CAPLUS
DOCUMENT NUMBER: 129:66838
TITLE: Transgenic non-human animals capable of producing heterologous antibodies
INVENTOR(S): Lonberg, Nils; Kay, Robert M.
PATENT ASSIGNEE(S): Genpharm International, USA
SOURCE: PCT Int. Appl., 453 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824884	A1	19980611	WO 1997-US21803	19971201
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CP, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 11206387	A2	19990803	JP 1998-126859	19910828
US 6300129	B1	20011009	US 1996-758417	19961202
AU 9856881	A1	19980629	AU 1998-56881	19971201
EP 942959	A1	19990922	EP 1997-953058	19971201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LV, FI, RO				
JP 2001527386	T2	20011225	JP 1998-525687	19971201

PRIORITY APPLN. INFO.:
US 1996-758417 A 19961202
US 1990-574748 B2 19900829
US 1990-575962 B2 19900831

JP 1991-515142 A3 19910828
 US 1991-810279 A2 19911217
 US 1992-853408 A2 19920318
 US 1992-904068 B2 19920623
 US 1992-990860 A2 19921216
 US 1993-53131 A2 19930426
 US 1993-96762 A2 19930722
 US 1993-155301 B2 19931118
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 US 1994-209741 B2 19940309
 US 1994-352322 A2 19941207
 US 1995-544404 A2 19951010
 US 1996-728463 A2 19961010
 WO 1997-US21803 W 19971201

AB The invention relates to transgenic non-human animals capable of producing heterologous antibodies and methods for producing human sequence antibodies which bind to human antigens with substantial affinity. The antigens described above are human carcinoembryonic antigen, human CD4, and human interleukin 8. The produced heterologous antibodies comprise a VH4-34 (or VH5-51) segment, a JH5 (or JH2) segment, a heavy chain CDR3 region comprising VINWFDP (or PANWNWYFVL), a VκL19 (or VκL18) segment, a Jκ2 (or Jκ4) segment, and a light chain CD3 region comprising the sequence QQANSFPYT (or QQPISYPQLT).

L3 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:435738 CAPLUS
 DOCUMENT NUMBER: 129:94468
 TITLE: Transgenic non-human animals capable of producing heterologous antibodies
 INVENTOR(S): Lonberg, Nils; Kay, Robert M.; et al.
 PATENT ASSIGNEE(S): GenPharm International, Inc., USA
 SOURCE: U.S., 173 pp. Cont.-in-part of U. S. 5,625,126.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 15
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5770429	A	19980623	US 1995-544404	19951010
WO 9203918	A1	19920319	WO 1991-US6185	19910828
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US				
RW: AT, BE, BF, BJ, CP, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
EP 814159	A2	19971229	EP 1997-201755	19910828
EP 814159	A3	19990714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 11206387	A2	19990803	JP 1998-126859	19910828
US 5569825	A	19961029	US 1991-810279	19911217
US 5789650	A	19980804	US 1992-853408	19920318
US 5545806	A	19960813	US 1992-990860	19921216
WO 9312227	A1	19930624	WO 1992-US10983	19921217
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CP, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 5814318	A	19980929	US 1993-96762	19930722
WO 9425585	A1	19941110	WO 1994-US4580	19940425
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JP 08140528	A2	19960604	JP 1994-289067	19941028
US 5625126	A	19970429	US 1994-352322	19941207
CA 2232813	AA	19970417	CA 1996-2232813	19961010
WO 9713852	A1	19970417	WO 1996-US16433	19961010
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RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CP, CG				
AU 9711149	A1	19970430	AU 1997-11149	19961010
AU 729290	B2	20010201		
EP 854917	A1	19980729	EP 1996-941938	19961010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1199422	A	19981118	CN 1996-197554	19961010
JP 200002324	T2	20000229	JP 1997-515285	19961010
US 6300129	B1	20011009	US 1996-758417	19961202
US 6255458	B1	20010703	US 1998-42353	19980313

PRIORITY APPLN. INFO.:

US 1990-574748 B2 19900829
 US 1990-575962 B2 19900831
 WO 1991-US6185 A 19910828
 US 1991-810279 A2 19911217
 US 1992-853408 A2 19920318
 US 1992-904068 A2 19920623
 US 1992-990860 A2 19921216
 WO 1992-US10983 A 19921217
 US 1993-53131 A2 19930426
 US 1993-96762 B2 19930722
 US 1993-155301 B2 19931118
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 US 1994-209741 B2 19940309
 WO 1994-US4580 A 19940425
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 JP 1991-515142 A3 19910828
 US 1992-834539 A2 19920205
 US 1995-544404 A 19951010
 US 1996-728463 A2 19961010
 WO 1996-US16433 W 19961010
 US 1996-758417 A2 19961202

AB The invention relates to transgenic non-human animals capable of producing heterologous antibodies and methods for producing human sequence antibodies which bind to human antigens with substantial affinity. Thus, demonstrated were construction of vector pGPe, IgM/IgG-expressing minilocus transgene pH2 encoding human VHI family gene VH49.8, redn. of

endogenous mouse Ig expression by antisense RNA, immunization and immune response (to dinitrophenyl and human carcinoembryonic antigen) in a transgenic mouse of present invention, targeted inactivation of murine .lambda. light chain locus and heavy chain locus, class switching and somatic mutation and B cell development in immunized transgenic mice homozygous for an inactivated endogenous Ig. locus and contg. HC1 or HC2 heavy chain transgenes, immunization with human CD4 and IgE, among others.

L3 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:361724 CAPLUS
 DOCUMENT NUMBER: 126:326445
 TITLE: Transgenic non-human animals capable of producing human or other heterologous antibodies specific for human antigens such as CD4
 INVENTOR(S): Lonberg, Nils; Kay, Robert M.
 PATENT ASSIGNEE(S): Genpharm International, Inc., USA; Lonberg, Nils; Kay, Robert M.
 SOURCE: PCT Int. Appl., 394 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 15
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9713852	A1	19970417	WO 1996-US16433	19961010
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
JP 11206387	A2	19990803	JP 1998-126859	19910828
US 5770429	A	19980623	US 1995-544404	19951010
AU 9711149	A1	19970430	AU 1997-11149	19961010
AU 729290	B2	20010201		
EP 854917	A1	19980729	EP 1996-941938	19961010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000502324	T2	20000229	JP 1997-515285	19961010
PRIORITY APPLN. INFO.:				
			US 1995-544404	A2 19951010
			US 1990-574748	B2 19900829
			US 1990-575962	B2 19900831
			JP 1991-515142	A3 19910828
			WO 1991-US6185	A 19910828
			US 1991-810279	A2 19911217
			US 1992-853408	A2 19920318
			US 1992-904068	A2 19920623
			US 1992-990860	A2 19921216
			WO 1992-US10983	A 19921217
			US 1993-53131	A2 19930426
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			US 1993-155301	B2 19931118
			US 1993-161739	B2 19931203
			US 1993-165699	B2 19931210
			US 1994-209741	B2 19940309
			WO 1994-US4580	A 19940425
			US 1994-352322	A2 19941207
			WO 1996-US16433	W 19961010

AB The invention relates to transgenic non-human animals capable of producing heterologous antibodies and methods for producing human sequence antibodies which bind to human antigens with substantial affinity. Several plasmid vectors are described and Ig-specifying DNA sequences are included. Esp., human CD4 antigen-specific antibodies are emphasized.

L3 ANSWER 7 OF 11 MEDLINE DUPLICATE 1
 ACCESSION NUMBER: 1998294464 MEDLINE
 DOCUMENT NUMBER: 98294464 PubMed ID: 9631008
 TITLE: High-avidity human IgG kappa monoclonal antibodies from a novel strain of minilocus transgenic mice.
 COMMENT: Comment in: Nat Biotechnol. 1996 Jul;14(7):826
 AUTHOR: Fishwild D M; O'Donnell S L; Bengoechea T; Hudson D V; Harding F; Bernhard S L; Jones D; Kay R M; Higgins K M; Schramm S R; Lonberg N
 CORPORATE SOURCE: Department of Hybridoma Development, GenPharm International, Mountain View, CA 94043, USA..
 SOURCE: NATURE BIOTECHNOLOGY. (1996 Jul) 14 (7) 845-51.
 PUB. COUNTRY: United States
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199807
 ENTRY DATE: Entered STN: 19980716
 Last Updated on STN: 19980716
 Entered Medline: 19980707

AB Human immunoglobulin transgenic mice provide a method of obtaining human monoclonal antibodies (Mabs) using conventional hybridoma technology. We describe a novel strain of human immunoglobulin transgenic mice and the use of this strain to generate multiple high-avidity human sequence IgG kappa Mabs directed against a human antigen. The light chain transgene is derived in part from a yeast artificial chromosome clone that includes nearly half of the germline human V kappa region. In addition, the heavy-chain transgene encodes both human mu and human gamma 1 constant regions, the latter of which is expressed via intratransgene class switching. We have used these animals to isolate human IgG kappa Mabs that are specific for the human T-cell marker CD4, have high binding avidities, and are immunosuppressive in vitro. The human Mab-secreting hybridomas display properties similar to those of wild-type mice including stability, growth, and secretion levels. Mabs with four distinct specificities were derived from a single transgenic mouse, consistent with an extensive diversity in the primary repertoire encoded by the transgenes.

L3 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 1996:502150 BIOSIS
 DOCUMENT NUMBER: PREV19969224506
 TITLE: High avidity human IgG-kappa anti-CD4 monoclonal

antibodies from a novel strain of minilocus transgenic mice.

AUTHOR(S): Fishwild, Dianne M.; O'Donnell, Susan L.; Bengoechea, Tasha; Hudson, Debra V.; Harding, Fiona; Bernhard, Susan L.; Jones, Debbie; Kay, Robert M.; Higgins, Kay M.; Schramm, Stephen R.; **Lonberg, Nils**

CORPORATE SOURCE: GenPharm Int., Mountain View, CA 94043 USA

SOURCE: Arthritis & Rheumatism, (1996) Vol. 39, No. 9 SUPPL., pp. S285.

Meeting Info.: 60th National Scientific Meeting of the American College of Rheumatology and the 31st National Scientific Meeting of the Association of Rheumatology Health Professionals Orlando, Florida, USA October 18-22, 1996

ISSN: 0004-3591.

DOCUMENT TYPE: Conference

LANGUAGE: English

L3 ANSWER 9 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2

ACCESSION NUMBER: 95109876 EMBASE

DOCUMENT NUMBER: 1995109876

TITLE: Over-expression of CD3.epsilon. transgenes blocks T lymphocyte development.

AUTHOR: Wang B.; Levelt C.; Salio M.; Zheng D.; Sancho J.; Liu C.-P.; She J.; Huang M.; Higgins K.; Sunshine M.-J.; Eichmann K.; Lacy E.; **Lonberg N.**; Terhorst C.

CORPORATE SOURCE: Division of Immunology, Beth Israel Hospital, Harvard Medical School, Boston, MA 02115, United States

SOURCE: International Immunology, (1995) 7/3 (435-448).

ISSN: 0953-8178 CODEN: INIMEN

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 021 Developmental Biology and Teratology

022 Human Genetics

026 Immunology, Serology and Transplantation

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We have reported previously that mice carrying >30 copies of the human CD3.epsilon. transgene completely lose their T lymphocytes and NK cells (36). Here we demonstrate by immunohistology that in the most severely immunodeficient mouse, tg.epsilon.26, the thymus is very small, has sizeable vacuoles and does not contain recognizable T lymphocytes except for a small percentage of Thy-1+ cells and B cells. Cell surface phenotyping and TCR.alpha. and -.beta. rearrangement studies confirm that the arrest in T lymphocyte development precedes the arrest in rag-1(null), rag-2(null) and TCR.beta.(null) mice. Since the T cell progenitors in which the arrest occurred were absent in the transgenic mice, indirect approaches were taken to examine the causes of the block in T cell development. Analyses of 12 independently established mutant mouse lines, generated with five different transgenic constructs, revealed that the severity of the abrogation in T cell development was dependent on the number of copies of transgenes. Since the number of transgene copies generally correlated with the levels of expression of the transgenic CD3.epsilon. proteins, we concluded that over-expression of the CD3.epsilon. protein was the likely cause of the block in T lymphocyte development. The T cell immunodeficiency was caused by either the human or the murine CD3.epsilon. protein. Since transgene coded mRNAs were found in significantly higher quantities than endogenous CD3.epsilon. mRNAs in fetal thymi on days 13 and 14 of gestation, over-expression took place very early in development, probably prematurely. Over-expression of the CD3.epsilon. transgene in thymocyte precursors may therefore affect T lymphocyte development in the absence of TCR and possibly in the absence of the other CD3 proteins. More importantly, over-expression of the CD3.epsilon. protein in thymocytes of mice with a low copy number of transgenes had a significant effect on late thymic development. Over-expression of the CD3.epsilon. protein in immature thymocytes mimicked the effects caused by exposure of CD4-CD8-thymocytes to anti-CD3.epsilon. treatment: apoptosis and lack of TCR.beta. expression. We therefore speculate that in the homozygous tg.epsilon.26 animals the arrest in T cell development was caused by excessive signal transduction events rather than by a toxic effect of the transgenic protein.

L3 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:689851 CAPLUS

DOCUMENT NUMBER: 123:81582

TITLE: Transgenic non-human animals expressing human immunoglobulin genes and capable of producing human antibodies by isotype switching

INVENTOR(S): **Lonberg, Nils**; Kay, Robert M.

PATENT ASSIGNEE(S): Genpharm International, Inc., USA

SOURCE: PCT Int. Appl., 295 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 15

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9425585	A1	19941110	WO 1994-US4580	19940425
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KR, KZ, LK, LU, LV, MG, MN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, CF, CG, CI, CM, GA, GN, ML				
JP 11206387	A2	19990803	JP 1998-126859	19910828
US 5814318	A	19980929	US 1993-96762	19930722
AU 9468194	A1	19941121	AU 1994-68194	19940425
JP 08509612	T2	19961015	JP 1994-524481	19940425
EP 754225	A1	19970122	EP 1994-916581	19940425
R: AT, BE, CH, DE, DK, ES, FR, GB, LI				
JP 08140528	A2	19960604	JP 1994-289067	19941028
US 5770429	A	19980623	US 1995-544404	19951010
PRIORITY APPLN. INFO.:			US 1993-53131	A 19930426
			US 1993-96762	A 19930722
			US 1993-155301	A 19931118
			US 1993-161739	A 19931203
			US 1993-165699	A 19931210
			US 1994-209741	A 19940309
			US 1990-574748	B2 19900829
			US 1990-575962	B2 19900831
			JP 1991-515142	A3 19910828
			WO 1991-US6185	A 19910828

US 1991-810279 A2 19911217
 US 1992-853408 A2 19920318
 US 1992-904068 A2 19920623
 US 1992-990860 A2 19921216
 WO 1992-US10983 A 19921217
 US 1993-156739 A 19931203
 WO 1994-US4580 A 19940425
 US 1994-352322 A2 19941207

AB Transgenic non-human animals capable of producing heterologous antibodies are prepd. and their use in the prepn. of antibodies that bind to human antigens with substantial affinity are described. These animals generate B cell precursors that present IgM on their surfaces and so are capable of maturing and are capable of isotype switching. Animals producing a single human antibody and not capable of isotype switching may also be prepd. The ability to recombine is ensured by taking care to ensure that sequences involved in the recombination process are introduced as part of the transforming DNA. The expression of endogenous Ig genes may be suppressed either by disruption of essential loci, by antisense methods, or using antibodies to endogenous Igs. Chimeric antibodies, e.g. with host organism const. regions, may also be prepd. if the endogenous genes are not inactivated. The construction of such genes and the prepn. of transgenic mice that synthesize and secrete human Igs is demonstrated. The prepn. of hybridomas secreting human monoclonal antibodies to CD4 antigen is also demonstrated.

L3 ANSWER 11 OF 11 MEDLINE DUPLICATE 3
 ACCESSION NUMBER: 88261303 MEDLINE
 DOCUMENT NUMBER: 88261303 PubMed ID: 3260331
 TITLE: Mouse brain CD4 transcripts encode only the COOH-terminal half of the protein.
 AUTHOR: Lonberg N; Gettner S N; Lacy E; Littman D R
 CORPORATE SOURCE: DeWitt Wallace Research Laboratory, Memorial Sloan-Kettering Cancer Center, New York, New York 10021.
 CONTRACT NUMBER: AI 23513 (NIAID)
 SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1988 May) 8 (5) 2224-8. Journal code: NGY; 8109087. ISSN: 0270-7306.
 PUB. COUNTRY: United States
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 OTHER SOURCE: GENBANK-M20265
 ENTRY MONTH: 198807
 ENTRY DATE: Entered STN: 19900308
 Last Updated on STN: 19970203
 Entered Medline: 19880729

AB The T-cell surface glycoprotein CD4 is thought to function as a receptor for class II major histocompatibility complex molecules. Human CD4 is also the lymphoid cell receptor for human immunodeficiency virus, the causative agent of acquired immune deficiency syndrome. The observed infection of the central nervous system in acquired immune deficiency syndrome patients raises the possibility that CD4 is also present in nerve tissue and that a cell surface receptor for class II major histocompatibility complex antigens could play a role in central nervous system function. This possibility is reinforced by the detection of unique CD4-related transcripts in mouse and human brain tissue. In this study, the structure of the mouse brain CD4 transcript was determined. It is identical to the last two-thirds of the CD4 message and is capable of encoding a 217-residue protein that would consist of a truncated, 154-residue, cell surface region, together with the complete CD4 transmembrane and cytoplasmic regions. It would not include an amino-terminal hydrophobic leader peptide.

=> s antibod? near CD4
 L4 0 ANTIBOD? NEAR CD4
 => s antibod? (P) CD4
 L5 41385 ANTIBOD? (P) CD4
 => s l5 and (10C5 or 4D1)
 L6 0 L5 AND (10C5 OR 4D1)
 => dis his

(FILE 'HOME' ENTERED AT 09:11:15 ON 14 MAR 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 09:11:41 ON 14 MAR 2002

L1 160 S LONBERG N?/AU OR KAY/AU
 L2 16 S L1 AND CD4
 L3 11 DUP REM L2 (5 DUPLICATES REMOVED)
 L4 0 S ANTIBOD? NEAR CD4
 L5 41385 S ANTIBOD? (P) CD4
 L6 0 S L5 AND (10C5 OR 4D1)

=> end
 ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
 LOGOFF? (Y)/N/HOLD:y
 COST IN U.S. DOLLARS

	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	42.22	42.37

	SINCE FILE	TOTAL
	ENTRY	SESSION
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	-4.34	-4.34

STN INTERNATIONAL LOGOFF AT 09:18:34 ON 14 MAR 2002

dis his

(FILE 'HOME' ENTERED AT 09:11:15 ON 14 MAR 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 09:11:41 ON 14 MAR 2002
L1 160 S LONBERG N?/AU OR KAY/AU
L2 16 S L1 AND CD4
L3 11 DUP REM L2 (5 DUPLICATES REMOVED)
L4 0 S ANTIBOD? NEAR CD4
L5 41385 S ANTIBOD? (P) CD4
L6 0 S L5 AND (10C5 OR 4D1)